

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule which comprises DNA having at least about 80% sequence identity to (a) a DNA molecule encoding a FGF-19 polypeptide comprising the sequence of amino acid residues from about 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a).

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2. The isolated nucleic acid molecule of Claim 1 comprising the sequence of nucleotide positions from about 464 or about 530 to about 1111 of Figure 1 (SEQ ID NO:1).

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3. The isolated nucleic acid molecule of Claim 1 comprising the nucleotide sequence of Figure 1 (SEQ ID NO:1).

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4. The isolated nucleic acid molecule of Claim 1 comprising a nucleotide sequence that encodes the sequence of amino acid residues from about 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2).

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5. An isolated nucleic acid molecule comprising DNA which comprises at least about 80% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219), or (b) the complement of the DNA molecule of (a).

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6. The isolated nucleic acid molecule of Claim 5 comprising DNA encoding the same mature polypeptide encoded by the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219).

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7. An isolated nucleic acid molecule comprising DNA which comprises at least about 80% sequence identity to (a) the full-length polypeptide coding sequence of the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219), or (b) the complement of the coding sequence of (a).

8. The isolated nucleic acid molecule of Claim 7 comprising the full-length polypeptide coding sequence of the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219).

5 9. An isolated nucleic acid molecule encoding a FGF-19 polypeptide comprising DNA that hybridizes to the complement of the nucleic acid sequence that encodes amino acids 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2).

10 10. The isolated nucleic acid molecule of Claim 9, wherein the nucleic acid that encodes amino acids 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2) comprises nucleotides 464 or about 530 to about 1111 of Figure 1 (SEQ ID NO:1).

11. The isolated nucleic acid molecule of Claim 9, wherein the hybridization occurs under stringent hybridization and wash conditions.

15 12. An isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least 80% positives when compared to the sequence of amino acid residues of from 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA of (a).

20 13. An isolated nucleic acid molecule comprising at least about 22 nucleotides and which is produced by hybridizing a test DNA molecule under stringent hybridization conditions with (a) a DNA molecule which encodes a FGF-19 polypeptide comprising a sequence of amino acid residues from 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a), and isolating the
25 test DNA molecule.

14. The isolated nucleic acid molecule of Claim 13, which has at least about 80% sequence identity to (a) or (b).

30 15. A vector comprising the nucleic acid molecule of any one of Claims 1 to 14.

16. The vector of Claim 15, wherein said nucleic acid molecule is operably linked to control sequences recognized by a host cell transformed with the vector.

~~17.~~ A nucleic acid molecule deposited with the ATCC under accession number 209480 (DNA49435-1219).

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18. A host cell comprising the vector of Claim 15.

19. The host cell of Claim 18, wherein said cell is a CHO cell.

10 20. The host cell of Claim 18, wherein said cell is an *E. coli*.

21. The host cell of Claim 18, wherein said cell is a yeast cell.

22. A process for producing a FGF-19 polypeptide comprising culturing the host cell of Claim 18 under conditions suitable for expression of said FGF-19 polypeptide and recovering said FGF-19 polypeptide from the cell culture.

~~23.~~ An isolated FGF-19 polypeptide comprising an amino acid sequence comprising at least about 80% sequence identity to the sequence of amino acid residues from about 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2).

24. The isolated FGF-19 polypeptide of Claim 23 comprising amino acid residues 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2).

25 ~~25.~~ An isolated FGF-19 polypeptide having at least about 80% sequence identity to the polypeptide encoded by the cDNA insert of the vector deposited with the ATCC on November 21, 1997 as ATCC Deposit No. 209480 (DNA49435-1219).

30 26. The isolated FGF-19 polypeptide of Claim 25 which is encoded by the cDNA insert of the vector deposited with the ATCC on November 21, 1997 as ATCC Deposit No. 209480 (DNA49435-1219).

27. An isolated FGF-19 polypeptide scoring at least 80% positives when compared to the sequence of amino acid residues from 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2).

28. An isolated FGF-19 polypeptide comprising the sequence of amino acid residues from 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2), or a fragment thereof sufficient to provide a binding site for an anti-FGF-19 antibody.

29. An isolated polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a FGF-19 polypeptide comprising the sequence of amino acid residues from 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a), (ii) culturing a host cell comprising said test DNA molecule under conditions suitable for the expression of said polypeptide, and (iii) recovering said polypeptide from the cell culture.

30. The isolated polypeptide of Claim 29, wherein said test DNA has at least about 80% sequence identity to (a) or (b).

31. A chimeric molecule comprising a FGF-19 polypeptide fused to a heterologous amino acid sequence.

32. The chimeric molecule of Claim 31, wherein said heterologous amino acid sequence is an epitope tag sequence.

33. The chimeric molecule of Claim 31, wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.

34. An antibody which specifically binds to a FGF-19 polypeptide.

35. The antibody of Claim 34, wherein said antibody is a monoclonal antibody.

36. The antibody of Claim 34, wherein said antibody is a humanized antibody.

37. The antibody of Claim 34, wherein said antibody is an antibody fragment.

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~~38.~~ An agonist to a FGF-19 polypeptide.

~~39.~~ An antagonist to a FGF-19 polypeptide.

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~~40.~~ A composition of matter comprising (a) a FGF-19 polypeptide, (b) an agonist to a FGF-19 polypeptide, (c) an antagonist to a FGF-19 polypeptide, or (d) an anti-FGF-19 antibody in admixture with a pharmaceutically acceptable carrier.

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~~41.~~ A method for screening for a bioactive agent capable of binding to FGF-19 comprising:

- a) adding a candidate bioactive agent to a sample of FGF-19; and
- b) determining the binding of said candidate agent to said FGF-19, wherein binding indicates a bioactive agent capable of binding to FGF-19.

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~~42.~~ A method for screening for a bioactive agent capable of modulating the activity of FGF-19, said method comprising the steps of:

- a) adding a candidate bioactive agent to a sample of FGF-19; and
- (b) determining an alteration in the biological activity of FGF-19, wherein an alteration indicates a bioactive agent capable of modulating the activity of FGF-19.

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43. A method according to Claim 42, wherein said biological activity is decreased uptake of glucose in adipocytes.

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44. A method according to Claim 42, wherein said biological activity is increased leptin release from adipocytes.

~~45.~~ A method of identifying a receptor for FGF-19, said method comprising combining FGF-19 with a composition comprising cell membrane material wherein said FGF-19 complexes with a receptor on said cell membrane material, and identifying said receptor as a FGF-19 receptor.

5 46. The method of Claim 45 wherein FGF-19 binds to said receptor, and said method further includes a step of crosslinking said FGF-19 and receptor.

47. The method of Claim 45, wherein said composition is a cell.

10 48. The method of Claim 45, wherein said composition is a cell membrane extract preparation.

~~49.~~ A method of inducing leptin release from adipocyte cells, said method comprising administering FGF-19 to said cells in an amount effective to induce leptin
15 release.

50. The method of Claim 49, wherein said FGF-19 is administered as a protein.

20 51. The method of Claim 49, wherein said FGF-19 is administered as a nucleic acid.

~~52.~~ A method of inducing a decrease in glucose uptake in adipocyte cells, said method comprising administering FGF-19 to said cells in an amount effective to
25 induce a decrease in glucose uptake.

53. The method of Claim 52, wherein said FGF-19 is administered as a protein.

30 54. The method of Claim 52, wherein said FGF-19 is administered as a nucleic acid.

55. A method of treating an individual for obesity, said method comprising administering to said individual a composition comprising FGF-19 in an amount effective to treat said obesity.

56. The method of Claim 55, wherein said treatment of obesity further results in the treatment of a condition related to obesity.

57. The method of Claim 55, wherein said FGF-19 is administered as a protein.

58. The method of Claim 55, wherein said FGF-19 is administered as a nucleic acid.

59. The method of Claim 55, wherein said composition further comprises a pharmaceutical acceptable carrier.

60. The method according to Claim 55, wherein said FGF-19 has at least about 85% amino acid sequence identity to the amino acid sequence shown in Figure 2 (SEQ ID NO:2).

61. A method of reducing total body mass in an individual, said method comprising administering to said individual an effective amount of FGF-19.

62. The method of Claim 61, wherein said FGF-19 is administered as a protein.

63. The method of Claim 61, wherein said FGF-19 is administered as a nucleic acid.

64. The method of Claim 61, wherein said FGF-19 is administered with a pharmaceutical acceptable carrier.

65. The method of Claim 61, wherein said reduction in total body mass includes a reduction in fat of said individual.

66. The method according to Claim 61, whererin said FGF-19 has at least about 85% amino acid sequence identity to the amino acid sequence shown in Figure 2 (SEQ ID NO:2).

67. A method of reducing the level of at least one of triglycerides and free fatty acids in an individual, said method comprising administering to said individual an effective amount of FGF-19.

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68. The method of Claim 67, wherein said FGF-19 is administered as a protein.

69. The method of Claim 67, wherein said FGF-19 is administered as a nucleic acid.

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70. The method of Claim 67, wherein said FGF-19 is administered with a pharmaceutical acceptable carrier.

71. The method according to Claim 67, whererin said FGF-19 has at least about 85% amino acid sequence identity to the amino acid sequence shown in Figure 2 (SEQ ID NO:2).

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72. A method of increasing the metabolic rate in an individual, said method comprising administering to said individual an effective amount of FGF-19.

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73. The method of Claim 72, wherein said FGF-19 is administered as a protein.

74. The method of Claim 72, wherein said FGF-19 is administered as a nucleic acid.

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75. The method of Claim 72, wherein said FGF-19 is administered with a pharmaceutical acceptable carrier.

76. The method according to Claim 72, wherein said FGF-19 has at least about 85% amino acid sequence identity to the amino acid sequence shown in Figure 2 (SEQ ID NO:2).

77. A rodent comprising a genome comprising a transgene encoding FGF-19.